pharmacopœial drug; and hence it is of ex-
ce that a student should know why many sub-
not used, or that are rarely used, should not
n the list of articles contained in the *Phar-*

nt's point of view the list of omissions is the
and most satisfactory feature in the new
There is a long list containing, I think, 188
sort and another that were included in the
f 1885, and are deleted from the *Pharmacopœia*
egard to this list of omissions a great deal of
ailed, and in some of the initial steps which
etions I had a large share. I feel satisfied in
e out, but I should have been better pleased
if we had whittled down the *Pharmacopœia* still further, and in looking over the list of omissions I do not for a moment regret the exclusion of any single drug or preparation.

The following question presented an initial difficulty: "On what principle is it to be decided that a drug is of no further value, or that its inclusion in the *Pharmacopœia* is no longer desirable?" While the first principle of the *Pharmacopœia* is to indicate the standard of purity of the substances used in medicine, there is no justification for retaining any drug that is not used with reasonable frequency by the general practitioner. Now with regard to the inquiries which were made by the Pharmacopœia Committee, much assistance was given by a large number of authorities, including the Royal College of Physicians of London, and the Society of Apothecaries of London, as recorded in the Preface. It was possible, however, that the opinions expressed were mainly those of teachers and consultants, and that they might scarcely represent the views of general practitioners. Information of great interest and of a more wide-spreading character resulted from private enterprise; I mean from such inquiries as were undertaken by Mr. Martindale, for instance, who had investigations made in several large centres of the last 2,000 copies of prescriptions of pharmacopœial substances. These indicated the number of times that a drug was used in these centres, and in that way a list was prepared which showed the degree of popularity attaching to each drug. This list is of value, but it fails just where the list of recommendations obtained from the different examining bodies had failed before; it does not indicate what the general practitioner uses. It is of very little use to consult the prescription books of chemists, which only show how often certain drugs are prescribed. We do not in that way find out the drugs used by the general practitioner; this analysis cannot represent what the doctor uses who dispenses his own drugs. Now, to meet that objection yet another investigation was undertaken by the Therapeutic Committee of the British Medical Association, and some of you may remember that a mysterious letter was sent round in which you were asked to indicate the relative frequency of your employment of certain drugs. It consisted of a table that was drawn up into three columns, marked:

Often.	Rarely.	Never.

Although from the first it was obvious that these lists contained numerous errors and must be used with discretion, they were of much service as an indication of the extent to which certain drugs had dropped out of use, and could therefore be omitted from the *Pharmacopœia*. To this inquiry, however, I shall have to refer more fully in my next lecture.

The French Medical School of Beyrout.—The Medical School of Beyrout, Asiatic Turkey, which is under the direction of Jesuit Fathers, has recently obtained a charter enabling it to grant licences to practise. The number of students has been steadily increasing for some years, and is now about 150. An extensive piece of land has recently been acquired, and on this site a new school is to be erected at an estimated cost of two millions of francs (£80,000). The French Government has promised a substantial subvention. A jury of examiners has recently been appointed, with Pro-
her members being
agrégé of the Paris
School of Constanti-
f Beyrout.

THE CHANGES IN THE CENTRAL NERVOUS SYSTEM OF TWO CASES OF NEGRO LETHARGY: SEQUEL TO DR. MANSON'S CLINICAL REPORT.

1899

[With Special Plate.]

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Two cases of Congo sickness, brought to England by Dr. Grattan Guinness, were admitted into Dr. Abercrombie's wards at Charing Cross Hospital last year, and for a short time were under my care; and a lecture with an account of these two cases was delivered by Dr. Manson, and reported in the British Medical Journal. These patients subsequently died, and the central nervous systems were handed to me for investigation. Before proceeding to describe the changes which were found, and which are illustrated in the accompanying micro-photographs, it will be well to remind my readers of the principal clinical phenomena presented by the patients during their illnesses. I am enabled to do this by making a summary from the case-book notes carefully abstracted by the house-physician Mr. Clogg, to whom I wish to express my obligations.

Case 1.—Eli Mboko, aged 20, was a Congolese school teacher of exceptional talent, speaking English perfectly, and having translated a book from English into his native language. His illness commenced twelve months before admission to the hospital on September 24th, 1898. Previously cheerful, interested in his avocation, he became vacant-minded and miserable, with little interest in his daily work, and as the disease progressed he would frequently fall asleep while at his work. These symptoms became more pronounced as time went on, but during his voyage to England he appears to have improved a little. Upon admission to the hospital, he was found to be fairly well nourished. The skin had to some extent lost its natural glossy condition, and there were a few papules over the abdomen. There was a general enlargment of the lymphatic glands, but they were discrete, and not anywhere massed together.

Nothing abnormal was found in the thorax or abdomen. Parchment scars on the fronts of both legs were evident. Examination of the eyes by Mr. Treacher Collins revealed nothing abnormal.

Examination of the fæces showed presence of the ova of the following parasites: Ankylostoma duodenale, trichocephalus dispar, ascaris lumbricoides (these parasites were treated successfully by anthelmintics). Examination of the blood by Dr. Manson on numerous occasions showed nothing markedly abnormal except the presence of the embryo filaria perstans, although there was some slight degree of anæmia.

The striking features to be associated with the nervous lesions, and which continued and progressed till the fatal termination, were:

1. Lethargy and a tendency to sleep the greater part of the day. From this drowsy condition the patient could always be aroused.

2. Slowness of speech without any tremor and without any noticeable change, except that there was an unwillingness to respond to questions owing to a sense of fatigue and drowsiness. The reaction time, as denoted by the time taken to frame an answer in response to a question, was much prolonged. When the patient spoke he usually made a curious grimace—elevation of the upper lip and nostrils.

3. Progressive motor enfeeblement, paresis like a man who had suffered a long illness. His gait also was that of weakness rather than paralysis or ataxy. He shuffled along, hardly lifting his legs from the ground, and with a wide base. Occasionally he would reel; there was nothing noteworthy about the reflexes, but the muscles, as indeed the whole body, were wasted, although the appetite was fairly good. There was no loss of sensation, and he complained of no definite pain except a pain in the back of the head, which he had had early in the illness. He suffered for some weeks with gingivitis.

4. The temperature until just towards the end of life, when hyperpyrexia occurred, was either normal, subnormal, or

[illegible] to the [illegible] of the [illegible] and the edge [illegible] [illegible] finger [illegible] below [illegible] case of the [illegible] [illegible] positive as [illegible] found to [illegible] [illegible] motor [illegible] more marked [illegible] [illegible] knee [illegible] [illegible] [illegible]

Examination [illegible] Dr. [illegible] present [illegible] [illegible] abdominal [illegible] proved [illegible] place [illegible] [illegible] aseptic syringe. [illegible]

The patient [illegible] [illegible] None of the cult[illegible] were therefore same [illegible] that [illegible] were contamin[illegible] [illegible] typical [illegible]

On February [illegible] right hand [illegible] were not [illegible] something [illegible] legs [illegible] [illegible]

On February [illegible] [illegible] right [illegible] eyelids opened and [illegible] were jerk[illegible] [illegible] at the elbow and wrist [illegible] The right leg then [illegible]

After [illegible] spasms [illegible] ceased [illegible] [illegible] between [illegible] yellow [illegible] During the [illegible] [illegible]

[illegible] very [illegible] [illegible] pneumonia [illegible] [illegible] physical examination [illegible] [illegible] observed only during the last [illegible] [illegible]

The following [illegible] cultures of the [illegible] made by Dr. H[illegible] with the exception of those [illegible] there was a small [illegible] diameter [illegible] abscess cavity [illegible] to contain a [illegible] Dr. Dam[illegible] [illegible] [illegible]

[illegible] I believe [illegible] that [illegible] it was [illegible] described with [illegible] [illegible] slightly raised, and the pulse denoted low arterial ure.

condition of the patient did not show any very marked ge until about three weeks before he died, when he was ed to breathe very deeply, and the alæ nasi could be seen king. Examination of the chest revealed nothing, but his h was very fœtid. He had no cough; respirations were more than 28. Two days before death a marked dys- occurred. Respirations now became 48 to 56, and were irregular. Only a little bronchitis and hypostatic conges- could be ascertained by physical examination, and his tem- ture rapidly rose on February 11th and continued until night of February 13th, when in the axilla the thermo- recorded 108 6°, and he died. His weight on admission 7 st. 3 lbs., at death 5 st. 7 lbs. The fœtid breath which red some weeks before his death could be accounted for fœtid expectoration which he coughed up. It was tur- blood-stained, and very foul; it no doubt came from an which was found *post mortem* in the lung. Whether it the cause of the hyperpyrexia or not it is difficult to say. ular tremors were observed only during the last hours of and there were never any fits or twitchings or periods of iacal excitement during the course of this patient's ss.

Necropsy.—The following is an abstract of the notes of the opsy made by Dr. Hunter. Body very emaciated; no mortis. All the organs, with the exception of those ioned especially may be considered as having presented mal appearances, although wasted. In the upper lobe of left lung there was a small nodule half an inch in diameter, ich on section proved to be a small abscess cavity taining thick pus, which on microscopical examination found to contain an immature disorganised parent worm. to this were two smaller abscesses. The pus-containing ities were close to a branch of the pulmonary artery, there was no connection, nor did there appear to be any nection between these abscess cavities and the bronchi. lungs otherwise appeared healthy. No ankylostomata nd in the duodenum. An adult filaria was found by Mr. Neil in the retroperitoneal tissue near the aorta, and also eral others at the root of the mesentery. These were bsequently identified by Dr. Manson as identical h those described by Dr. Daniels as occurring in the k Indians of British Guiana. The heart was very all, weighed only 5½ ozs., and the muscle had a pale hyaline pearance. Central nervous system: Removal of the skull- p; the calvarium dense and hard, rather thin, symmetrical. a mater not adherent, longitudinal sinus empty. No ked excess of cerebro-spinal fluid, ventricles neither dilated granular. Slight pia-arachnoid thickening; right hemi- here, weight 1 lb. 6ozs.; left, 1 lb. 6 ozs.; cerebellum, 6 ozs. volutions not wasted. complex, and to all appearances a y well-formed brain. The spinal cord and spinal ganglia wed nothing abnormal to the naked eye. They were pre- rved in 5 per cent. formalin, and subsequently the portions ere hardened in various fluids for microscopical examina- ion.

The change which I believe essential to this disease was nd in both cases. and will be described with the next case.

CASE II.—Tenda Mkaloo, aged 11, admitted September 24th, 98. This patient was unable to speak English, and his fellow ferer conversed with him and for him. Supposed date of ill- ss three or four months prior to admission. He was carried to the hospital partly on account of his weakness, partly on count of his drowsy condition. Weight 3 st. 11 lbs. Very aciated, and there was a certain amount of proptosis, for e eyelids did not meet during sleep, the sclerotics being ible. Skin dry and lustreless, covered on the thorax and domen with numerous papules. Marked pruritus, slight njunctivitis and excessive lachrymal secretion. Marked ibbling of saliva, fœtid breath, tongue furred but moist; ps dry and covered with dry epithelium. Hair was not nged red; he was evidently full of fear, and whether this as the cause of his disinclination to palpation or whether it as actual pain could not be discovered. There was general ndular enlargement, as in the other case, only more rked. He constantly put his hand to his neck, which ap- ared to pain him; the cervical glands were much enlarged. orax, heart, and lungs normal; abdomen uniformly enlarged and flaccid; spleen, extended to the level of the umbilicus, was hard and smooth, and the edge sharp, not tender. Edge of liver could be felt three fingers' breadths below the costal margin, sharp; surface of the liver smooth, not tender. Fæces contain the same parasite as Case I. Eyes, examined by Mr. Treacher Collins, found to be normal.

The patient presented the same characteristic features as regards mental and motor enfeeblement (but more marked), combined with lethargy, and a mounful expression, as Case I, except that the knee-jerks were slightly exaggerated and plantar reflexes brisk; moreover, towards the end of life epileptiform convulsions, contracture of the limbs, retraction of the head and neck, unconsciousness, and Cheyne-Stokes breathing developed, but no hyperpyrexia.

Examination of the blood by Dr. Manson showed the presence of the embryo filaria perstans, but nothing else noteworthy is recorded. The intestinal parasites were cleared out with thymol, and his general condition and weight improved. Decrease in size of the liver, spleen, and lymphatic glands took place. Six weeks after admission some cervical glands were removed by Mr. Boyd, and 5 c.cm. of blood was withdrawn from the median basilic vein in the arm by means of an aseptic syringe. No benefit resulted from operation.

Dr. Bulloch placed 2½ c.cm. into each of two tubes of bouillon. He also attempted to make cultures from the gland on glycerine agar. None of the cultures had grown at the end of three weeks, he therefore came to the conclusion that no ordinary micro-organisms were contained in the blood or glands. Neither could I by staining sections show tubercle bacilli in the glands. I regret, however, that lumbar puncture was not performed and cultures taken from the cerebrospinal fluid.

On February 4th a fine tremor of the right hand developed, and a few days later a tremor of left arm and hand. The gums became spongy, and there was a foul smelling discharge from the mouth. A little later retraction of the head and neck occurred, and he began to pass his urine under him. Then on February 14th contracture of thighs on abdomen and legs on thighs noted, and he was frequently found crying and moaning as if in great pain. The knee-jerks were active, and there was no ankle clonus. His appetite failed, and he could only take fluid nourishment.

On February 21st the first fit occurred, and was succeeded in twelve hours by seventy-five others. They started with conjugate deviation of head and eyes to the right, the right side of the face was drawn, the jaws were at first clenched; the eyelids opened and closed very quickly, and the eyeballs were jerked from side to side. The arm was next flexed at the elbow and wrist, and the fingers flexed into the palm. The right leg then became rigid.

After the clonic spasm there was relaxation of the right side, and the left side passed through a tonic and clonic stage. At first the convulsions lasted for from 2½ to 3 minutes, and they followed one another in rapid succession. Later there was a greater interval between the fits, and they were of shorter duration, and did not extend to the left side of the body. The breathing in the interval between the fits (when there was any interval) was at first quite regular and shallow, about 24 per minute. During the two following days the patient had 23 more fits, making altogether 98 in three days. The temperature during the fits was 103° on an average. The breathing became irregular, and was at one time typical Cheyne-Stokes. The patient was completely unconscious during the fits, also during the intervals which were short, but when, later, a longer interval took place, he became semiconscious. Occasional irregular spasms followed, twitching of the face muscles, especially of the left side and risus sardonicus, with a peculiar catching breathing as if there were spasm of the diaphragm. Bedsores began to appear on the trochanters and sacrum. On March 12th patient appeared to be in great pain, crying out frequently, so that he had to be placed in a special ward. He had to be fed by the nasal tube. On March 19th patient had 94 more fits, similar to those previously described. He continued to have epileptiform fits, and later there appeared to be paresis of the right facial muscle and arm, as he was never seen to move the latter, although he did his left arm. On March 19th the temperature became subnormal, never rising above 96° until his death on April 2nd.

During the last few days of his life he had several fits a day, and the rigidity seemed to pass off in a measure. He was quite unconscious at the end, and appeared to have paralysis of the muscles of deglutition.

Necropsy.—The following is the report of a *post-mortem* examination made by Dr. Hunter: Body extremely emaciated, weight 3 stone. Bedsores on all prominences. Relations of organs in the thorax and abdomen natural. Mesenteric glands enlarged. No pleural or peritoneal effusions. Bronchial glands enlarged. Right lung, lower lobe exhibits a consolidated patch with recent lymph on pleural surface. On section this appears like a tuberculous mass with circumscribed pneumonia. Discrete nodules, shot-like to feel, exist throughout the lungs. No cysts or abscesses. Heart small, muscle shows brown pigmentation. Kidneys small, each 2½ ounces, natural appearance. Thyroid, spleen, stomach normal, also intestines, with exception of duodenum, which shows a few patches of congestion here and there. Liver apparently normal in appearance. Bladder normal.

The brain was taken out soon after death. The dura mater was adherent to the calvarium. The cerebro-spinal fluid was slightly turbid, but colourless and in excess. The pia arachnoid over the convexities was thickened and opaque, but could be stripped without erosions, no marked flattening of convolutions nor wasting. The ventricles were not dilated and the ependyma was not granular. The spinal cord and ganglia were removed and appeared healthy except at the lower part where there was inflammation of the meninges due to extension from the large and very deep sacral bedsore. No doubt the gelatinous yellow deposit around the roots of the cauda equina was due to extension of septic inflammation from the bedsore. The cerebro-spinal fluid was examined for micro-organisms by cultures, etc., and various organisms including diplococci, streptococci pyogenes, and bacilli were found, but, of course, under the circumstances no importance could be attached to these observations. Embryo filar a were found alive in this fluid (which, however, contained a little blood) thirty-six hours after removal from the body. Both in this case as well as Case I the pituitary body was in all respects normal. In both cases after hardening in 5 per cent. formalin the central nervous system and especially the medulla showed marked puncta cruenta. The vessels of the brain in neither showed any naked-eye abnormality. Portions of the brain, basal ganglia, pons, medulla, spinal cord, cerebellum, and spinal ganglia were hardened respectively in alcohol, Muller's fluid, Marchi's fluid, and 5 per cent. formol, and after fixation were embedded in celloidin or paraffin; thin sections were cut and stained by Nissl, Marchi, and Marchi-Pal methods. The microscopical appearances in both cases exhibited essentially similar but not identical conditions. There were in both instances lepto-meningitis and encephalo-myelitis. Throughout the whole central nervous system, but especially in the medulla and at the base of the brain, sections showed the pia arachnoid infiltrated with mononuclear leucocytes, the inflammation could be traced along the blood vessels and septa into the substance of the nervous system (*vide* Figs. 1, 2, 10).

The perivascular lymphatics around both large and small vessels were crowded with these lymphocytes. The left cerebral hemisphere of Case II showed a more intense inflammation than the right, and the infiltration of the membranes was more marked, which very probably may be associated with the right-sided fits, especially as one found in the motor region of this side more disorganisation of cells (*vide* Fig. 8).

Sections were stained by Gram, Pfeiffer, and many other methods for micro-organisms, but with negative results. Considering the universal evidence of intense chronic inflammation, the wonder is that the ganglion cells did not present more marked evidence of disorganisation. By Nissl method the cells of the cerebral cortex in the motor region of Case I showed a normal outline, but scattered through the substance, especially in the pericellular spaces, are the small round nucleated cells (*vide* Fig 9). In all other parts of the nervous system of Case I the outline of the cells is fairly normal, but owing to the hyperpyrexia characteristic bio-chemical change had taken place in all the nerve cells. The Nissl bodies were neither visible in the cells nor upon the processes, the whole neuron being uniformly stained by the dye instead of the normal differentiation into achromatic and chromatic substances (*vide* Figs. 6, 7, 9). The columns of Meynert were preserved, and if there had been no hyperpyrexia I doubt if much change would have been visible in the neurons.

In Case II the cortex cerebri, especially of the left sid showed more marked cellular, but not very much more marked perivascular, changes. The columns of Meynert were disorganised, the outline of a great many of the pyramidal cells, large as well as small, altered and irregular, indicating disorganisation and destruction (*vide* Fig. 8, and compare with Fig. 9 from Case I). In the spinal cord and various other parts of the central nervous system numbers of cells of fairly normal appearance existed, and in these the Nissl bodies appeared natural (*vide* Fig. 3). The medulla showed to the naked eye marked congestion of the vessels; and, microscopically examined, the evidence of chronic inflammatory reaction around the vessels and in the membranes was profound. Very many of the nerve cells were shrunken and atrophied, others showed chromatolysis, and not many normal cells were discoverable (*vide* Fig. 11).

Fibres.—Sections of the brain and spinal cord were stained by Marchi and Marchi-Pal methods. Nothing abnormal was found in Case I, with perhaps the exception that the tangential and supraradial fibres were not quite so numerous as normal. In Case II there was obvious atrophy of both these sets of fibres, and also to a less degree of the interradial fibres in the motor regions of both hemispheres, but especially the left (*vide* Figs. 12 and 13).

Examination of the spinal cord showed no degeneration or sclerosis in Case I, whereas in Case II there was a slight diffuse sclerosis (*vide* Fig. 5) in the pyramidal tracts, especially of the right side, with recent degenerated fibres. There was no degeneration in the anterior or posterior roots. The arteries showed no endarteritis in either case, but in the choroid plexus there were numerous psammomata, caused, I believed, by degenerated and occluded vessels. The epithelium appeared quite normal. The spinal ganglia showed the same evidence of a chronic inflammatory process; but with the exception of the hyperpyrexial change of Case I, the cells appeared otherwise fairly normal. The central canal of the spinal cord was filled up with proliferated glia tissue in both cases.

REMARKS.

The condition common to both cases was a meningo-encephalo-myelitis. MM. Regis and Gaide[2] have attributed the symptoms to a diffuse meningo-encephalitis of infective origin. They described, however, the clinical symptoms only of a case observed in the region of Timbuctoo; but, so far as I know, this is the first detailed microscopical examination which has been made.

With the exception of the lymphatic glands and duodenum, the examination of the other viscera revealed nothing noteworthy. Sections of the lymphatic glands showed a proliferation of lymphocytes, and section of the duodenum showed also a large number of lymphocytes, and increase of size of the lymphoid nodules.

Both the clinical history and the morbid appearan point to a chronic process. It only affects negroes in We Africa, and it is here, though not exclusively, that t filaria perstans occurs. We might therefore attribute it this parasite, but to my mind the evidence is insuffici Some authorities have thought that it might be due to b food, thus resembling in its etiology pellagra and lathyri This is not altogether unlikely, for there are certain clini features resembling pellagra. Possibly it is due to so infectious organism for which a suitable stain has not been found.

I will, however, not speculate further upon the patho of the disease, although I cannot refrain from pointing out t in my opinion the poison acts especially upon the lymph system, and particularly that of the central nervous syst The lethargy, together with progressive motor and mental feeblement could be explained either by the action of a to agent, circulating in the cerebro-spinal fluid, upon the vi activities of the neurons, or simply by the accumulati of lymphocytes around all the blood vessels interferi with the metabolic exchanges between the blood and t nervous elements. Although the existence in such abu ance of mononuclear leucocytes would rather indic the existence and prolonged action of a noxious ag

would be capable of damaging the nervous ele- The mechanical theory, however, has some support, that a somewhat similar condition of drowsy stupor, ssive paresis, and dementia, with epileptiform convul- may be brought about by internal hydrocephalus occa- by tumour of the third ventricle. Whether the hyper- in Case I can be attributed solely to the encephalo- I cannot say, seeing that there was a fœtid abscess in but I think it is quite possible. The right-sided fits, cular tremors, and the contracture in Case II were un- dly due to the inflammatory changes, with irritation, destruction of the nervous elements in the cerebral especially of the left hemisphere.

her question might be asked: Is this a nervous station of constitutional syphilis, akin to general is, which also by some authorities is considered a primary meningo-encephalitis. The geographical demiological character of the disease, together with the of granular ventricles and the universal inflammatory ion, is against this hypothesis, although sections motor cortex of Case II might upon microscopical ation pass for general paralysis; but I have never, in t acute forms of general paralysis, seen so much general an inflammatory condition of the vessels; yet ve-cell changes of this disease, which may last years, ht in comparison with that other almost invariably disease, general paralysis. This offers to my mind a argument in favour of the theory that general paralysis primary degeneration of the neuron with secondary matory changes.

her Dr. Bulloch's observations nor my own support the ations and experiments of MM. Gagigal and Lepierre, hed in the *Comptes Rendus de la Société de Biologie*, y, 1898, in which they claim to have isolated a bacillus the blood which grows upon serum, upon gelatine, and llon. These authors claim to have produced the disease mals, but MM. Brault and Lapin obtained some of the es, and were unable to confirm the results (sur logie et la Pathogénie de la Maladie du Sommeil, *de Parasitologie*, etc., July, 1898. Again. M. Marchand du Pneumocoque dans la Pathologie de la Maladie du eil, *Annales de l'Institut Pasteur*, March, 1899) attributes disease to the pneumococcus, rather by inference than Still, I regret that Quincke's lumbar puncture was not med and the cerebro-spinal fluid tested as I ted.

negative evidence obtained by Dr. Bulloch and myself rds micro-organisms does not preclude the possibility the disease is due to a living organism, for no organism been discovered in rabies, nor has a specific organism found for syphilis.

able confirmation of these observations has been af- me by the courtesy and kindness of Dr. Stephen nzie. Having read the very interesting clinical report case under his care in 1890, published in vol. xxiv of the al Society's *Transactions*, I wrote asking him if any scopical examination of the central nervous system had made. He kindly sent me a box of specimens in ad- le preservation. The collection contained sections of of the organs and included sections of the occipital and o-sphenoidal lobes, also of the corpus striatum. The mens were stained with carmine and logwood and eosin; showed the same evidence of chronic meningo-en- litis that I have detailed in the above cases. All the scular spaces were crowded with mononuclear leuco- ; but the method of hardening and staining employed not lend itself to a study of the condition of the nerve It is therefore highly probable that meningo-encephal- the constant lesion of this disease.

conclusion, I wish to express my indebtedness to Dr. and Dr. Grattan Guinness for giving me the opportu- of making the above investigation.

DESCRIPTION OF PHOTO-MICROGRAPHS.

1.—Anterior median fissure of lumbar enlargement, Case I. Con- gested vessel and membranes infiltrated with mononuclear leuco- cytes. Magnification 150 diameters.

2.—Section of medulla, Case I. Stained by Nissl method, showing perivascular lymphatics, greatly distended and filled with mono- clear leucocytes. The blood in the small vessel in the centre shows five leucocytes. Magnification 250 diameters.

Fig. 3.—Anterior horn cell from the first sacral segment, Case II. Stained by Nissl method. Magnification 600 diameters. This shows a fairly normal cell; the Nissl bodies are seen upon the dendrons and in the body of the cell. The surrounding tissue shows a large number of leucocytes, and the chronic inflammatory changes in the vessels and membranes were very intense, yet there were many cells in the section as normal in appearance as this one, although there were some which showed some change in the chromophilous substance.

Fig. 4.—Central canal of the spinal cord, cervical region. Stained by Nissl method. Magnification 100 diameters. The canal is filled up with proliferated glia tissue, and there is a proliferation of the ependymal cells; exactly the same condition was found in Case II.

Fig. 5.—Cross pyramidal tract showing slight sclerosis and recent (black) degenerated fibres. Mid-dorsal region of spinal cord, Case II; right side. Magnification 200 diameters.

Fig. 6.—Anterior horn cell first sacral segment, Case I. Stained by Nissl method: magnification 600. There is no abnormality in the form of the cell, but the Nissl bodies are absent on the processes and in the body of the cell, the whole "neuron" being stained a uniform dull diffuse purple. The nucleus is especially distinct and unstained; the nucleolus deeply stained. This change was undoubtedly due to the hyperpyrexia, and is in no way connected with the disease. The cells throughout the central nervous system showed this acute change brought about by the high fever. If the patient had died suddenly from some other cause it is my opinion that the Nissl reaction of the cells would have been normal. Contrast Figs. 3 and 6. There are far more leucocytes in the surrounding tissue in Fig. 3.

Fig. 7.—Medium-sized pyramidal cell from the third layer of the motor cortex, Case I. Nissl staining, magnification 750 diameters. There is chromatolysis. and the whole cell is stained a diffuse purple, consequently no Nissl bodies are evident on the processes. Two mononuclear leucocytes can be seen close to the body of the cell, and many others were observable on altering the focus. A dark strand can be seen passing from the apical dendron through the body of the cell and out by the axon, doubtless continuous fibrillæ, which are made evident by the pathological change.

Fig. 8.—Section of sensori-motor cortex, Case II. Stained by Nissl method. Magnification 200. The columns of Meynert are not seen; the cells are irregular in shape. Their processes are broken off; the small vessels are congested; and the appearances are not unlike those of acute general paralysis; but no spider cells were seen in the superficial layers. Contrast this with Fig. 9.

Fig. 9.—Section of sensori-motor cortex, Case I. Stained by Nissl method. Magnification 200. The cells are of good shape, although imperfectly and diffusely stained. The apical processes are of normal outline, and the columns of Meynert are not destroyed. There are numerous capillaries surrounded by deeply-stained leucocytes, and the same are seen in the perivascular lymph spaces.

Fig. 10.—Occipital region of cortex cerebri, Case II. Magnification 150 diameters. Perivascular lymphatic is seen in the subcortical white matter filled and and distended with mononuclear leucocytes; also a large number in the surrounding tissue. It may be here remarked that every vessel in the whole nervous system showed appearances more or less as marked as this.

Fig. 11.—Section of medulla, Case II. Stained by Nissl method. Magnification 250 diameters. Two small veins cut obliquely are seen side by side, with the perivascular sheath distended and filled with mononuclear leucocytes: in the neighbourhood are some nerve cells shrunken, and with their processes gone, apparently in a degenerating condition.

Fig. 12.—Section of sensori-motor cortex, Case I, stained by Marchi-Pal method. Magnification 200 diameters. The horizontal tangential fibres which lie on the surface of the convolutions, and which correspond to the axons of the molecular layer of Cajal, are seen in fair abundance. Contrast with Fig. 13.

Fig. 13.—Section of sensori-motor cortex, Case II. Stained by Marchi-Pal method. Magnification 200 diameters. The tangential fibres are here almost entirely destroyed. It is probable that the decay and death of these cortical structures was associated with the epileptiform fits which occurred in the later period of the illness.

REFERENCES.

[1] December 3rd, 1898, p. 1672. [2] *Presse Médicale*, October 1st, 1898.

REPORT ON AN OUTBREAK OF TYPHOID FEVER AT SHOEBURYNESS ATTRIBUTED TO EATING COCKLES.

BY

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SHOEBURYNESS is an urban district at the extreme south-east of the county of Essex, bounded on the south by the Thames, on the east by the German Ocean, and on the north and west by the Rochford Rural District, of which until recently it formed a part. Nearly the whole of this area has a high death-rate from typhoid fever, and every autumn outbreaks of greater or less intensity occur.

The population of Shoebury at the last census was 2,990, but